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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,334	07/18/2000	MICHEL DROUX	PH-98/080	6869

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	16

DATE MAILED: 06/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/486,334	Applicant(s) DROUX ET AL.	
	Examiner Anne Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-7,9-13,15-26 and 31-71 is/are pending in the application.

4a) Of the above claim(s) 7,10,11,15,16,21,22 and 31-59 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-6,9,12,13,17-20,23-26 and 60-71 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendments to the specification, the amendments to claims 2-6, 9, 12-13, 17-20, 23-25, the cancellation of claims 1, 8, 14 and 27-30, and the addition of new claims 60-70 requested in Paper No.13, filed 28 March, 2002, have been entered.

2. In the response filed 28 March, 2002, Applicant again argued the restriction requirement on the grounds that the different serine acetyltransferase (SATase) sequences have corresponding technical features and relate to a single inventive concept under PCT rule 13.1.

This is not found persuasive. The technical feature shared by the groups is overexpression, by any method, of a SAT in plants. This technical feature is taught in the art (see 102 rejection in the prior office action). Thus, the restriction requirement is still deemed proper and therefore remains FINAL. Applicant is required to delete references to non-elected enzymes and sequences.

Claims 7, 10-11, 15-16, 21-22 and 31-59 remain withdrawn from consideration, as being drawn to nonelected inventions. Claims 2-6, 9, 12-13, 17-20, 23-26 and 60-71 are examined to the extent they read on SEQ ID NO:1, which encodes the *Arabidopsis* cytoplasmic SATase, SAT3.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The disclosure remains objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. In the response filed 28 March, 2002, Applicant urges that pg 41, line 15, of the specification contains the web address of an internet program and that is not a form of browser-executable code (response pg 15). This is not found persuasive

because "http://" followed by a URL address is an example of an embedded hyperlink. See MPEP § 608.01.

5. The proposed drawing corrections submitted 28 March , 2002, have been accepted. Corrected formal drawings are required in reply to this Office action to avoid abandonment of the application. This requirement will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

6. The copy of the specification submitted with the response filed 28 March, 2002, has not been entered because there was no direction in that response to do so. All amendments to the specification were entered into the specification as originally filed.

A substitute specification is still required pursuant to 37 CFR 1.125(a) because dark smudges on the pages could result in printing errors.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

Thus, the substitute specification must include the amendments made in the response filed 28 March, 2002.

Response to Arguments

7. The rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Saito et al, 1994, in view of Noji et al and further in view of Ruffet et al is WITHDRAWN in light of arguments by Applicant that Ruffet et al teaches SAT5.

Response to Amendment

8. The rejections of claims 1, 4-6, 8, 12-13 and 24 under 35 U.S.C. 102(b) as being anticipated by Takahashi et al and of claims 1-3, 6, 8 and 24 under 35 U.S.C. 102(b) as being anticipated by Saito et al in light of Noji et al are WITHDRAWN in light of amendments to the claims to indicate that the plants and plant cells have been transformed with a nucleic acid encoding serine acetyltransferase.

9. The rejection of claims 1-6, 8-9, 12-13, 17-20 and 23-30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is WITHDRAWN in light of amendments making the method steps circular.

Claim Rejections - 35 USC § 112

10. Claims 2-6, 9, 12-13, 17-20, 23-26 and 60-71 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by transformation with a gene encoding a cysteine-insensitive plant SATase, does not reasonably provide enablement for methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by transformation with a nucleic acid encoding a

cysteine-sensitive SATase, by mitochondrial transformation with the nucleic acid, for mutagenesis of a plant SATase, for plant transformation with a protein, or for chloroplast targeting via use of an optimized transit peptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 10 September, 2002, as applied to claims 1-6, 8, 12-13, 17-20 and 23-30.

Applicant's arguments filed 28 March, 2002, have been fully considered but they are not persuasive. Applicant urges that the SATs are well characterized and a number of genes encoding them have been cloned, and that the figures of the specification disclose suitable SAT genes. Applicant also urges that methods of cloning SAT genes are known in the art and described in the specification, and that SAT genes are described in the specification on pg 6 and 9 and in the figures. Applicant also urges that methods for cloning SAT genes are known in the art and described in the examples of the specification. Applicant urges that Example 9 and Figure 12 disclose a vector suitable for expression of any SAT in the cytoplasm of a plant. Applicant urges that overexpression in the mitochondria (claim 12) can be accomplished via a mitochondrial signal peptide/SAT fusion protein. Applicant urges that pg 9, lines 14-27 of the specification teach cysteine-sensitive and cysteine-insensitive SATs. Applicant urges that chloroplast targeting via an optimized transit peptide (OTP) is taught on pg 14, line 18, to pg 15, line 5 and shown in Figure 11 (response pg 15-17).

This is not found persuasive. None of the references on pg 6 or 9 of the specification nor any sequences in the sequence listing or in the figures teach any plant SAT gene other than from *Arabidopsis*. The specification does not describe the hybridization and wash conditions or the

PCR hybridization conditions, or the probes or primers needs to isolate SAT genes from any organism other than *Arabidopsis*. Thus, the claims are not enabled for genes encoding SATases from any plant.

The instant specification fails to provide guidance for methods of increasing the production of cysteine, glutathione, methionine and any sulfur derivative by overexpression of a cysteine-sensitive SATase. The instant specification even states that cysteine induced inhibition of SATase is a limiting factor in the synthesis of cysteine (pg 8, lines 4-10). As no working examples are provided of overexpression of a cysteine sensitive SATase resulting in increased production of cysteine, unpredictability is not overcome.

Claim 12 encompasses mitochondrial transformation, which neither the instant application nor the art teach. It is suggested that the claim be amended to indicate that a nucleic acid encoding a mitochondrial signal peptide/SAT fusion protein is used.

The claims, as amended, are drawn to a method of transforming plant cells with a SAT protein (see claim 60). Neither the instant specification nor the art teach plant transformation with a protein. It is suggested that the claims be amended so that the plant cells are transformed with a nucleic acid encoding a serine acetyltransferase.

Claim 5 is drawn to a method of overexpressing a mutated plant SATase. The instant specification, however, fails to provide guidance for which amino acids of the SATase can be altered and to which other amino acids, and which amino acids must not be changed, to convert a cysteine-sensitive SATase to a cysteine-insensitive one.

Neither the specification on pg 14, line 16 to pg 15, line 5, nor EP 508 909 teach the DNA sequence that encodes the OTP. Additionally, the unpredictability associated with the use of any targeting sequence, as detailed in the prior Office action, has not been overcome.

11. Claims 17, 19, 23, 25, 60 and 70-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 10 September, 2002, as applied to claims 1, 6, 17,19, 23, 25 and 27-30.

Applicant's arguments filed 28 March, 2002, have been fully considered but they are not persuasive. Applicant urges that the OTP is disclosed in the specification at pg 14, line 16 to pg 15, line 5 and in EP 508 909, and that an OTP is not essential for practicing the instant invention (response pg 17-18).

This is not found persuasive because neither the specification on pg 14, line 16 to pg 15, line 5, nor EP 508 909 teach the DNA sequence that encodes the OTP. Additionally, claim 71 is drawn to use of an OTP. Thus, a deposit is still required, as detailed in the prior Office action.

12. Claims 2-6, 12-13, 17-20, 23-26 and 60-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 10 September, 2002, as applied to claims 1-6, 8, 12-13, 17-20 and 23-30.

Applicant's arguments filed 28 March, 2002, have been fully considered but they are not persuasive. Applicant urges that SAT is a well-characterized enzyme and that the specification describes 6 *Arabidopsis* SAT genes. Applicant urges that one could substitute other SAT genes by reference to the scientific literature and databases. Lastly, Applicant urges that an OTP is disclosed as discussed above (response pg 18-19).

This is not found persuasive because the specification does not teach SAT genes from any plant other than *Arabidopsis*. The specification also does not describe mutant SAT genes and cysteine-insensitive SATs from any plant. Lastly, as detailed in the enablement rejections above, the specification does not teach the sequence of an OTP.

See *In re Shokal*, 113 USPQ 283, (CCPA 1957) at pg 285

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary. ...
> We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

13. Claims 2-6, 9, 12-13, 17-20, 23-26 and 60-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 10 September, 2002, as applied to claims1-6, 8-9, 12-13, 17-20 and 23-30, and for the new reasons detailed below.

Applicant's arguments filed 28 March, 2002, have been fully considered but they are not persuasive.

Claims 4 remains indefinite in its recitation of the abbreviation "SAT", as stated in the prior Office action. Applicant urges that claims have been amended to remove the abbreviation "SAT". This is not found persuasive because the abbreviation remains.

Claim 26 remains indefinite in its recitation of the abbreviation "EPSPS", as stated in the prior Office action. Applicant urges that the abbreviation is well-known in the art. This is not found persuasive because it is not defined in the specification.

Claim 20 is indefinite in its recitation of "the serine acetyltransferase and transit peptide ... are homologous". Applicant urges that homologous and heterologous are defined on pg 13 of the specification. This is not found persuasive because they are not so defined. If Applicant wishes to indicate that the serine acetyltransferase and transit peptide are from the same organism or that the transit peptide is from a serine acetyltransferase gene, or is from the same gene as the serine acetyltransferase, or have the same sequence, the claim should be so amended.

Similarly claim 23 is indefinite in its recitation of "SAT is heterologous with the transit peptide". Applicant urges that homologous and heterologous are defined on pg 13 of the specification. This is not found persuasive because they are not so defined. If Applicant wishes to indicate that the serine acetyltransferase and transit peptide are from different organisms or that the transit peptide is not from a serine acetyltransferase gene, but is from the same organism, or have different sequences, the claim should be so amended.

Claim 60 is indefinite in the recitation of "plant cells transformed with a serine acetyltransferase", as plants are not transformed with proteins but with nucleic acids.

Claim Rejections - 35 USC § 103

14. Claims 2-6, 12-13, 17, 19-20, 23-26 and 60-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al in view of Noji et al. The rejection is repeated for the reasons of record as set forth in the Office action mailed 10 September, 2002, as applied to claims 1-6, 8, 12-13, 17, 19-20 and 23-30.

Applicant's arguments filed 28 March, 2002, have been fully considered but they are not persuasive. Applicant urges that Saito et al found no significant changes in cellular content of cysteine and glutathione in the transgenic plants, and that Saito et al concluded that cellular contents of cysteine and glutathione were stable under normal growth conditions. Applicant urges that Noji et al does not suggest over expression of SAT in plants to increase production of cysteine. Applicant urges that Saito et al has nothing in common with the instant invention because they use a different enzyme. Applicant urges that the rejection represents hindsight reasoning (response pg 23-26).

This is not found persuasive because Saito et al do state that "an increase in 3F and 4F plants was observed" (pg 891, left column, paragraph 1). Saito et al also suggest overexpression of serine acetyltransferase (pg 893, left column, paragraph 1); Noji et al teach genes encoding that enzyme.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (*i.e.*, cysteine overproduction, as opposed to cysteine, glutathione, methionine or sulfur-containing derivatives of methionine, and normal growth conditions) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

15. Claim 18 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al, 1994, in view of Noji et al as applied to claims 2-6, 12-13, 17, 19-20, 23-26 and 60-71 above, and further in view of Svab et al. The rejection is repeated for the reasons of record as set forth in the Office action mailed 10 September, 2002.

Applicant's arguments filed 28 March, 2002, have been fully considered but they are not persuasive. Applicant urges that Svab has nothing in common with the instant invention and do not cure the deficiencies of Saito et al, 1994, in view of Noji et al (response pg 27-28).

This is not found persuasive for the reasons indicated above. Svab et al teach plastid transformation in tobacco (pg 914-915), and the introduction of protein into the chloroplast by chloroplast transformation or by nuclear transformation with a construct that has a chloroplast transit peptide is an obvious design choice.

16. Claim 9 is free of the prior, art, given the failure of the prior art to teach or suggest a method of increasing the production cysteine, glutathione, methionine or sulfur-containing derivatives of methionine in plants by transformation with a nucleic acid encoding SEQ ID NO:2.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kimberly Davis, at (703) 305-3015.

Anne R. Kubelik, Ph.D.
June 12, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638